Fall risk in people with MS:

a physiological profile assessment study

Multiple Sclerosis Journal - Experimental, Translational and Clinical

doi: 10.1177/2055217316641130 Date of acceptance: 1st March 2016

Embargo period: None

Phu D Hoang, PhD¹, Meryem Baysan², Hilary Gunn³, PhD, Michelle Cameron⁴, Jenny Freeman³, PhD, Jennifer Nitz PhD⁵, Nancy L Low Choy PhD^{5,6}., Stephen R Lord, PhD¹

- 1. Neuroscience Research Australia and University of New South Wales, Sydney Australia
- 2. Nijmegen Medical Centre, Radboud University, Nijmegen, The Netherlands
- 3. School of Health Professions, Plymouth University, United Kingdom
- 4. Oregon Health & Science University and VA Portland Health Care Service, Portland, Oregon, USA
- 5. School of Health Sciences, The University of Queensland, Brisbane, Australia
- 6. School of Physiotherapy, The Australian Catholic University (McAuley), Brisbane Australia

⊠ Corresponding Author:

Professor Stephen Lord, Neuroscience Research Australia, PO Box 1165, Randwick NSW, 2031, Sydney,

Australia.

Email: s.lord@neura.edu.a

Phone: 61 2 9399 1061

Fax: 61 2 9399 1204

Running Title: Fall risk in MS

ABSTRACT

Introduction: The Physiological Profile Assessment (PPA) is used in research and clinical practice for assessing fall risk. We compared PPA test performance between people with Multiple Sclerosis (MS) and healthy controls, determined the fall-risk profile for people with MS and developed a reference database for people with MS.

Methods: 416 ambulant people with MS (51.5±12.0 years) and 352 controls (52.8±12.2 years) underwent the PPA (tests of contrast sensitivity, proprioception, quadriceps strength, reaction time and sway) with composite fall risk scores computed from these measures. MS participants were followed prospectively for falls for three months.

Results: The MS participants performed significantly worse than controls in each PPA test. The average composite fall-risk score was also significantly elevated indicating a "marked" fall-risk when compared to controls. 155 MS participants (37.3%) reported 2+ falls in the follow-up period. Frequent fallers performed significantly worse than non-frequent fallers in the contrast sensitivity, reaction time and sway tests and had higher PPA composite scores. **Conclusions:** In line with poor PPA test performances, falls incidence in people with MS was high. This study provides comprehensive reference data for the PPA measures for people with MS that could be used to inform future research and clinical practice.

Word count = 199

INTRODUCTION

Falls are common among people with multiple sclerosis (MS) and knowledge about fall risk factors in MS has increased significantly in the last decade. About 60% of people with MS will fall at least once and more than 30% will fall three or more times across a three to twelve month period¹⁻³. Identified risk factors associated with falls include advanced disease status^{1, 3, 4}, balance impairments^{2, 5, 6}, slow choice stepping reaction time, reduced walking speed,

reduced executive functioning², weakness in the lower limbs⁶, use of walking aids⁶⁻⁸, fear of falling^{9, 10}, forgetfulness⁹, bladder incontinence⁹ and fatigue¹¹.

A number of tests have been used to estimate fall risk in this group. These have included clinical assessments such as the Berg Balance Scale (BBS) and the Timed Up and Go (TUG) Test ¹² and laboratory-based tests such as posturography involving moving force-plates and visual surrounds¹³. There is some evidence that the clinical assessments can discriminate between people with MS who do and do not fall^{14, 15} but these tests have limitations in that they are restricted to measures of functional balance, and not broad ranging physiological impairments. It has been shown the BBS has a ceiling effect in higher functioning adults¹⁶ and the predictive capacity of the TUG test is at best moderate in community ambulant older people¹⁷. Other simple tools, such as the Physiological Profile Assessment (PPA)¹⁸ may complement functional balance tests and have value in evaluating fall risk in people with MS^{2, 3}.

The PPA provides quantitative measures of key physiological risk factors for falls, including lower limb strength, sensation, balance during quiet standing, vision and hand reaction time. The PPA was designed to be low-tech, portable, simple and quick to administer and able to produce valid and reliable quantitative measures¹⁶. The PPA generates quantitative scores for each test domain as well as a summed, weighted total risk score. PPA component and fall risk scores have been shown to have good predictive ability of falls in community-dwelling older people and clinical groups including people with MS^{2, 3}.

The aims of this study were to a) examine whether PPA component and composite test performance scores discriminate between frequent and non-frequent fallers in people with MS, b) compare these scores of people with MS with data from age-matched healthy controls and c) develop a reference database of PPA fall risk scores for people with MS. These findings could help identify people with MS at increased risk of falling and be used to evaluate the effectiveness of fall prevention programs aimed at improving physical performance outcomes.

METHODS

Protocol Approvals and Participant Consent

The data used in the current analysis were obtained from prospective cohort studies of fall risk in people with MS carried out in Australia (AUS), United Kingdom (UK) and the United States (US). These studies were approved by local ethics committees and written informed consent was obtained from all participants.

MS Participants

Data from 416 people with MS were included in this analysis: 210 participants from AUS, 148 from the UK and 58 from the US. Common inclusion criteria for all samples were: a) participants were diagnosed with MS using standardized criteria for MS diagnosis^{19, 20} and b) participants were aged 18 years and older without restriction of any MS subtypes. Common exclusion criteria were inability to understand and sign an informed consent or being unable to follow test instructions.

Additional inclusion criteria for the Australian sample were ability to stand unsupported for 30 seconds and ability to walk 10 meters with or without a mobility aid (i.e. Disease Steps 0- 5^{19} , Appendix 1). The UK participants were restricted to an EDSS score between 3.5 and 6.5, and full recovery from any recent relapse was required for inclusion. The US sample included participants with an EDSS score of 6.0 or less, an upper age limit of 50 years, being relapse free for 30 days prior to baseline examination, and ability to walk at least 100 meters. EDSS

was assessed either face-to-face by a trained clinician or by self-report using a telephone interview²⁰. Disease severity was measured by the EDSS²¹ in the samples from the UK and the US. In Australia the Disease Steps scale¹⁹ was used and converted to EDSS by mobility criteria.

The Australian sample was recruited from an outpatient MS physiotherapy clinic in Sydney. Participants in the UK sample were recruited via invitation letters from their local neurologist and an advertisement in the newsletter of the South West Impact of MS (SWIMS) project, which is accessed by over 1500 people with MS living in the South West of England²². The US sample was recruited from patients receiving medical care at specialty MS center outpatient clinics at a Department of Veterans Affairs medical center and a university medical center, and from the surrounding area, in the Northwest of the United States.

Demographic information including age, gender, number of years diagnosed with MS and type of MS was collected using a structured questionnaire. Trained therapists also assessed participants' level of disability (EDSS scores²¹ or Disease Steps¹⁹).

Control participants without MS

Data for 352 age-matched healthy participants were randomly selected from the databases of research studies conducted at Neuroscience Research Australia^{23, 24} and the University of Queensland²⁵⁻²⁸. Participants for these studies were generally representative of the general population and were recruited via the electoral roll, health insurance databases and convenience sampling. Exclusion criteria were: having a neurological condition such as MS, Parkinson's disease or stroke, an MMSE score < 24 (indicating probable dementia)²⁹ and speaking no or very little English.

Physiological Profile Assessment (PPA)

The Physiological Profile Assessment (PPA) comprises five sensorimotor and balance measures: visual contrast sensitivity, proprioception, quadriceps muscle strength, hand reaction time, and postural sway.

Visual contrast sensitivity was assessed using the Melbourne Edge Test, which presents 20 circular patches containing edges with reducing contrast. Correct identification of the orientation of the edge on the patches provides a measure of contrast sensitivity in decibel units, where $1 \text{ dB} = 10 \log 10$ contrast. Proprioception was measured using a lower-limb toe matching test, where difference (in degrees) in matching the great toes was recorded using a vertical clear acrylic sheet inscribed with a protractor placed between the legs. The proprioception test was administered as quickly as possible and rest periods were provided between trials to minimise fatigue influencing the test. Quadriceps muscle (isometric) strength in kilograms was examined in the more affected leg using a spring gauge while participants were seated with the hip and the knee joints at 90° of flexion. Hand reaction time in milliseconds was assessed using a light as a stimulus and a finger-depression of a switch as the response. Postural sway area (maximal anterior-posterior and medio-lateral sway in mm) was quantified using a sway-meter that measured the displacement of the body at waist level while participants stood for 30 seconds on a foam rubber mat with their eyes open. This area measurement was subsequently converted to an estimate of sway path (a more precise measure and better discriminator of fall risk in both older people and people with $\mathrm{MS}^{2,\,18}$) using a regression equation from large population studies.

The five PPA components were weighted to compute a composite PPA fall risk score expressed in standard (z-score) units. In studies of older people, PPA fall risk index scores discriminate between multiple and non-multiple fallers with accuracies up to 75%, with scores of less than 0 indicating a low risk of falling, 0 to 1 indicating a mild risk, 1 to 2

indicating a moderate risk, and scores of 2 indicating a high risk of falling.

Falls definition and follow up

In this study two fall definitions were used. For the sample from Australia a fall was defined as "unintentionally coming to the ground or other lower level and other than a consequence of sustaining a violent blow, loss of consciousness, sudden onset of paralysis as in stroke or epileptic or seizure³³⁰. For samples from the UK and US a fall was defined as "a slip or trip in which participants came to rest on the ground or floor or lower level³¹. Following the assessment, participants were asked to prospectively record any falls in the next three months using a diary system³². Participants received monthly falls diary sheets, written instructions and reply-paid return envelopes. A reminder telephone call or email was sent to participants whose diary returns fell behind schedule³². Previous studies of older people have found that recurrent falls are more likely to indicate physiological impairments and chronic conditions than single falls, and are therefore more clinically important. In line with previous studies, frequent fallers were defined as those who had ≥ 2 falls in the follow-up period³.

Statistical analysis

Descriptive data for the PPA component tests and composite risk scores are presented. These include percentiles for those aged 20-39, 40-49, 50-59 and \geq 60 years. The proprioception, quadriceps strength, reaction time and sway variables were positively skewed, and were log transformed to allow further parametric analyses. Pearson correlations were used for assessing PPA performance scores, age, and years since MS diagnosis. Group t-tests were used to compare the differences in these measures between men and women, between prospective fallers and non-fallers, and between frequent fallers (two or more falls in three months) and non-frequent fallers (zero or one falls in three months). Finally, PPA

performance scores were contrasted between the MS sample and age-matched healthy controls without MS using General Linear Models, adjusting for age and gender. Data were analyzed with SPSS (version 22) for Windows (SPSS, Chicago, IL, USA).

RESULTS

Demographic characteristics of the MS sample

Demographic characteristics of the sample are presented in Table 1. The MS sample (n =416) comprised 305 women (73.3%) and 111 men (26.7%) with mean age 51.5 years (SD = 12.0, range = 21-84) and mean years since MS diagnosis 13.7 (SD=9.9). The men and women were of similar age 50.8 (SD = 13.0) and 51.8 (SD = 11.6); $t_{1,414}$ =0.76, p=0.45). The mean EDSS of the sample was ~ 4 (range = 0 - 6.5). Approximately 62.0% of the sample was diagnosed with relapse-remitting MS, 23.8% with secondary progressive MS, 13.5% with primary progressive MS and 0.9% unknown.

Comparison with age-matched controls without MS

The age-matched control participants without MS sample (n =352) comprised 274 women (77.8%) and 78 men (22.2%) with mean age 52.8 years (SD = 12.2, range = 21-84). There were non-significant trends for the MS sample to be younger (51.5 (SD-12.0) years vs. 52.8 (SD=12.2) years, $t_{1,766}$ =1.44,p=0.150 and and comprise fewer women (73.3% vs. 77.8%, χ^2 =2.10,df=1,p=0.15) than the control group. The participants with MS performed significantly worse than the control participants without MS in each of the PPA tests and had higher PPA composite scores, after adjusting for age and gender in general linear model analyses (Table 2). Figure 1 shows mean PPA composite scores for the age-bands presented in the MS PPA reference database in relation to composite score norms for healthy control participants without MS²⁵⁻²⁸.

PPA reference values for people with MS

Reference data for both men and women for the five PPA tests and composite fall risk scores are presented in Table 3. Men performed similarly to women in all tests, with the exception of knee extension strength: 36.7 ± 14.5 and 23.6 ± 91 kg force respectively ($t_{1,414}$ =10.2, p<0.001). Performances in all PPA tests were significantly associated with years since diagnosis of MS and performance in all PPA tests, with the exception of proprioception, were significantly associated with age (Table 4).

PPA test scores in relation to MS subtypes and disease severity

Mean ages (SD) for the three MS subtype groups were as follows: Relapsing Remitting - 47.0 (11.4) years, Secondary Progressive -59.2 (8.8) years and Primary Progressive 58.5 (8.9) years (p<0.001). The proprotions of particiants in the three groups who were women were 74.3%, 72.7% and 67.9% respectively (p=0.61). Table 5 shows the PPA test measures for participants with Relapsing Remitting, Secondary Progressive and Primary Progressive MS. Significant between-group differences were evident for the visual contrast sensitivity, knee extension strength and postural sway tests and PPA composite scores when adjusting for age.

Figure 2 shows the relationship between PPA composite scores and EDSS categories (Figure 2). The Pearson correlation coefficient for this association was 0.478 (p<0.001), and this was only slightly attenuated when adjusting for age in a partial correlation analysis; r=0.405, (p<0.001). PPA and EDSS scores did not differ significantly by gender (p=0.103 and p=0.792 respectively).

Prospective falls

All MS participants completed the three month follow-up fall calendars. Two hundred and

twenty six (226) participants (54.4%) reported having at least one fall in the three month follow-up period; 71 (17.1%) fell once, 46 (11.1%) fell twice, 25 (6.0%) fell three times, 22 (5.3%) fell four times and 62 (14.9%) fell \geq 5 times. There were 1,350 reported falls in total. Table 6 shows the PPA test measures for those who reported 0, 1, 2 and 3+ falls during follow-up. Frequent (2+) fallers performed significantly worse than the non-frequent fallers in the visual contrast sensitivity, hand reaction time and postural sway tests and had higher PPA composite scores. The proportion of participants who suffered multiple falls increased with increasing composite PPA scores, i.e. 25.0% in those with scores \leq 0, 27.4% in those with scores > 0 and \leq 2, 37.5% in those with scores > 2 and \leq 3 and 56.4% in those with scores > 3; $\varkappa^2=28.4$, df=3, p<0.001. The area under the receiver-operator characteristic score for the composite PPA – frequent faller association was 0.64.

DISCUSSION

Our study compared fall risk scores of people with MS to those of a healthy control population and examined whether PPA component and composite test performance scores discriminated between frequent and non-frequent fallers in this population. We found that the MS sample performed significantly worse than the age-matched control participants without MS in all PPA tests. Overall, 62% of the MS sample had PPA scores of one or higher (moderate fall risk) and 47% had PPA scores of two or higher (high fall risk). This indicates that most people with MS are at an increased fall-risk when compared to normative data, and as shown in figure 1, fall risk is significantly elevated across the adult lifespan.

Fall risk was also evident by the high fall rate reported with over 50% of the cohort reporting one or more falls and over 37% reporting two or more falls in the three month follow-up. Frequent fallers performed significantly worse than the non-frequent fallers in three of the five component tests: visual contrast sensitivity, hand reaction time and postural sway, and had higher PPA composite scores. In contrast, there were only trends for the MS sample to have reduced lower limb proprioception and knee extension strength. This suggests these measures may be less important for fall risk in people with MS compared with older people – the population group in which the PPA was developed. For knee extension strength, in particular, it appears that performance may be adequate in both frequent and non-frequent fallers in people with MS.

PPA composite score were significantly associated with EDSS scores when adjusting for age, and differing fall risk profiles for people with different MS sub-types. The Relapsing Remitting group performed best in all PPA tests, and significant between-group differences were evident for the visual contrast sensitivity, knee extension strength and postural sway tests and PPA composite scores. Noticeably, the Secondary Progressive group had significantly poorer knee extension strength than both the Relapsing Remitting and Primary Progressive groups and may be a distinguishing risk factor for this group.

Strengths of this analysis include the rigorous prospective falls surveillance and the recruitment of a large sample drawn from three countries with EDSS scores ranging from one to 6.5, covering ambulatory people with few symptoms to those with major balance and gait impairments. We also acknowledge that while the physiological tests were able to distinguish frequent fallers from non-frequent fallers, the area under the receiver-operator characteristic score for the composite PPA – frequent faller association was only moderate, and there are undoubtedly other general and disease-specific measures such as strength of other muscle groups, fine motor control, spasticity, fatigue and dynamic balance steps (such as voluntary and reactive stepping) that may have provided additional insight into the fall risk profile in people with MS. Further research could provide additional reference data to add to the current fall risk profile. Second, due to the differing methods of recruitment within both the

MS and healthy control groups, it is not possible for us to present data on response rates. Third, while no participants were unable to complete the lower limb proprioception test due to not being fully able to extend either leg due to weakness or fatigue, it is acknowledgment that as this test involved movements against gravity, test results may have bee affected by reduced muscle strength in some participants. Finally, the data presented for sway path are indirect as they were estimated from a regression equation from measured maximal anterior-posterior and lateral sway measurements from the swaymeter. This more robust measure was included in the reference database as it can now be measured simply with a mobile application (www.neura.edu.au/apps/ppaswaypath) as used in a recent randomized controlled trial²⁶

Clinical implications and conclusions

This study illustrates the value of a physiological profiling approach to identifying sensory and motor impairments and documenting overall reduced physiological performance in people with MS²⁵. The compiled reference database for the PPA component and composite scores should assist future studies using the PPA in evaluating balance performance and evaluating effectiveness of interventions in people with MS. Further, as the PPA comprises simple "low tech" tests it has scope for widespread use in clinical settings.

Acknowledgements: Phu Hoang was funded by Multiple Sclerosis Research Australia; Simon Gandevia and Stephen Lord were funded by National Health and Medical Research Council (NHMRC) Australia. Michelle Cameron was funded by the US Department of Veterans Affairs Rehabilitation Research & Development Service. Hilary Gunn and Jenny Freeman were funded by a grant from the Physiotherapy Research Foundation (Chartered Society of Physiotherapy, UK)

Figure 1: Mean PPA composite scores for the age-bands presented in the MS PPA reference database in relation to composite score norms for healthy control participants without MS.

The light blue curved band shows the PPA composite score range across the life span for healthy people without MS – top border indicating 75th percentile and bottom border 10th percentile. Superimposed on this established relationship are scores for people with MS in age-groups 20-39,40-49, 50-59 and 60+ years. The middle of the bubble points indicate the age-group mean scores, and the bubble size indicates the age-group standard deviations.

	Australia	UK	United States	Total sample
	(n=210)	(n=148)	(n=58)	(n=416)
Age in years: Mean (range)	50.3 (21-73)	58 (33-84)	39.5 (22-50)	51.5(21-84)
Gender: (F:M)	150:60	114:34	41:17	305:111 (73:27)
(Ratio %)	(71:29)	(77:23)	(71:29)	
Years with MS	13.6	16.7	6.5	13.7
(SD)	(8.9)	(10.9)	(5.8)	(9.9)
EDSS:	3.66	5.0	2.6	4.03
Mean (range)	1.0 - 6.5	3.5 - 6.5	0 - 6.0	0 - 6.5
Subtype RRMS SPMS PPMS Unknown	160 (76.2%) 30 (14.3%) 19 (9.0%) 1 (0.5%)	42 (28.4%) 66 (44.6%) 37 (25%) 3 (2%)	55 (94.8%) 3 (5.2%) 0 0	257 (61.7%) 99 (23.8%) 56 (13.5%) 4 (0.9%)

Table 1: Demographic characteristics of each sample from the three countries

EDSS: Expanded Disability Status Scale, RRMS: Relapsing Remitting Multiple Sclerosis; SPMS: Secondary Progressive Multiple Sclerosis; PPMS: Primary Progressive Multiple Sclerosis

Test measure	People with MS Mean	Non-MS controls
	(SD), N=416	Mean (SD), N=352
Visual contrast sensitivity (dB)	21.2 (2.5)	22.0 (2.2)**
Proprioception (° error)	3.6 (2.6)	2.0 (1.4)***
Knee extension strength (kg force)	27.1 (12.3)	30.5 (12.4)***
Hand Reaction Time (ms)#	300 (99)	244 (57)***
Sway path (mm)#	586 (896)	112 (54)***
PPA composite score#	2.15 (1.87)	0.00 (1.11)***

Table 2: PPA test and composite scores: MS – control group comparisons

* - p < 0.05, *** p<0.001, adjusted for age and sex.

Control group N=212, due to measure not included in all control group studies Note: low visual contrast sensitivity and knee extension strength scores and high proprioception, reaction time, sway and high PPA composite scores indicate impaired performance

Test	Age-	10%	25%	50%	75%	90%
	group					
Visual contrast sensitivity						
(dB)						
	20-39	19.8	21.0	22.0	24.0	24.0
	40-49	18.0	21.0	22.0	24.0	24.0
	50-59	18.0	21.0	22.0	24.0	24.0
	60+	16.6	20.0	21.0	22.0	24.0
Proprioception (° error)						
. ,	20-39	1.4	2.0	2.8	3.8	4.9
	40-49	1.4	2.0	2.8	3.8	4.9
	50-59	1.4	2.1	3.3	5.7	9.7
	60+	1.4	2.1	3.3	5.7	9.7
Knee extension strength (kg force)						
	20-39	25.4	35.0	44.0	62.0	69.2
	40-49	22.0	30.3	39.0	48.0	54.0
	50-59	14.9	28.5	36.0	45.5	52.0
	60+	14.9	22.0	28.0	34.0	40.0
Reaction time (ms)						
	20-39	192	210	229	262	314
	40-49	208	217	261	300	495
	50-59	214	227	265	317	469
	60+	214	227	265	345	469
Sway (mm)						
	20-39	72	97	118	369	729
	40-49	76	119	196	369	729
	50-59	117	145	268	490	995
	60+	123	145	268	490	995
PPA score						
	20-39	-0.54	-0.47	0.83	2.09	3.32
	40-49	-0.47	0.25	1.53	2.73	3.93
	50-59	0.39	0.91	1.93	3.32	5.23
	60+	0.40	0.91	1.93	3.32	5.43

Table 3a: Reference values (percentiles) for PPA component and composite fall risk scores for the MS sample – men

Note: low visual contrast sensitivity and knee extension strength scores and high proprioception, reaction time, sway and PPA composite scores indicate impaired performance.

tor the Mis sample						
Test	Age-	10%	25%	50%	75%	90%
	group					
Visual contrast						
sensitivity (db)						
	20-39	20	21	22	24	24
	40-49	19	21	22	24	24
	50-59	19	20	21	22	24
	60+	17	19	21	22	23
Proprioception (° error)						
	20-39	1.0	1.6	2.4	3.3	5.0
	40-49	1.0	1.6	2.8	4.4	7.4
	50-59	1.0	1.6	2.8	5.0	7.7
	60+	1.0	1.8	3.6	5.4	7.7
Knee strength						
	20-39	17.0	20.0	25.0	32.0	40.0
	40-49	13.0	20.0	25.0	32.0	40.0
	50-59	13.0	17.0	23.0	28.0	34.0
	60+	9.6	14.5	20.0	26.0	31.2
Reaction time (ms)						
	20-39	211	224	246	294	342
	40-49	214	230	266	312	394
	50-59	215	245	298	374	460
	60+	220	252	314	852	890
Sway (mm)						
	20-39	80	110	153	351	703
	40-49	80	122	203	412	995
	50-59	98	149	264	700	1020
	60+	143	202	314	853	1160
PPA score						
	20-39	-0.28	0.08	1.06	2.03	4.12
	40-49	-0.10	0.51	1.29	2.92	4.61
	50-59	0.12	0.99	2.29	3.74	4.95
	60+	0.86	1.66	2.41	4.08	5.60

Table 3b: Reference values (percentiles) for PPA component and composite fall risk scores for the MS sample – women

Note: low visual contrast sensitivity and knee extension strength scores and high proprioception, reaction time, sway and PPA composite scores indicate impaired performance

	MS duration	Age
Visual contrast sensitivity (dB)	240***	280***
Proprioception (° error)	.120**	.081
Knee extension strength (kg force)	228***	314***
Hand Reaction Time (ms)	.171***	.227***
Sway path (mm)	.244***	.240***
PPA score	.289***	.312***

Table 4: Correlations between physiological and functional tests and duration of MS disease and age

Note: low visual contrast sensitivity and knee extension strength scores and high proprioception, reaction time, sway and PPA composite scores indicate impaired performance ** p<0.01, *** p<0.001

Test measure	Relapsing	Secondary	Primary	Р*
	Remitting	Progressive	Progressive	
	Mean (SD)	Mean (SD)	Mean (SD)	
Visual contrast	21.8 (2.0)^	20.2(2.6)	20.6 (3.7)	.002
sensitivity (dB)				
Proprioception (° error)	3.4 (2.39)	4.0 (2.9)	3.9 (3.2)	.590
Knee extension strength	29.0 (13.0)^	21.8 (8.5)~	27.7 (12.1)	.007
(kg force)				
Hand Reaction Time	289 (93)	321 (113)	310 (80)	.485
(ms)				
Sway path (mm)	477 (815)^#	814 (1051)	702 (907)	.004
PPA composite score	1.73 (1.77)^#	2.94(1.80)	2.69 (1.94)	.002

 Table 5: PPA test and composite scores: MS sub-group comparisons

* p value for F statistic adjusted for age

^ Relapsing Remitting vs. Secondary Progressive (p<0.05)

~ Secondary Progressive vs. Primary Progressive (p<0.05)

Relapsing Remitting vs. Primary Progressive (p<0.05)

Note: low visual contrast sensitivity and knee extension strength scores and high proprioception, reaction time, sway and PPA composite scores indicate impaired performance

Table 6. PPA	test and compo	site scores: f	faller group	comparisons#
Table 0. FFA	test and compe	site scores. I	laner group	comparisons

Table 0. 1171 test and com	bosite sectes. Iun	er group compa	150115	
Test measure	0 falls	1 fall	2 falls	3+falls
	N=190	N=71	N=46	N=109
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Visual contrast sensitivity	21.7 (1.9)	21.4 (2.0)	20.5 (2.9)	20.6 (3.2)***
(dB)				
Proprioception (° error)	3.6 (2.6)	3.1 (2.3)	3.3 (2.4)	3.9 (2.9)
Knee extension strength	27.3 (12.0)	28.1 (13.4)	26.4 (12.1)	26.4 (12.2)
(kg force)				
Hand Reaction Time (ms)	292 (85)	291 (77)	301 (112)	318 (118)*
Sway path (mm)	514 (871)	307 (428)	734 (910)	832 (1078)***
PPA composite score	1.87 (1.80)	1.66 (1.39)	2.54 (2.06)	2.80 (2.00)***

Number of falls participants suffered in the 3 month follow-up

Group t-tests comparing test scores for non-frequent (0,1) and frequent (2+) fallers; * p<0.05, *** p<0.001

Note: low visual contrast sensitivity and knee extension strength scores and high proprioception, reaction time, sway and PPA composite scores indicate impaired performance

REFERENCES

1. Nilsagard Y, Gunn H, Freeman J et al. Falls in people with MS-an individual data meta-analysis from studies from Australia, Sweden, United Kingdom and the United States. *Mult Scler* 2015; 21:92-100.

2. Hoang PD, Cameron MH, Gandevia SC et al. Neuropsychological, balance, and mobility risk factors for falls in people with multiple sclerosis: a prospective cohort study. *Arch Phys Med Rehabil* 2014;95:480-6.

3. Gunn H, Creanor S, Haas B et al. Risk factors for falls in multiple sclerosis: an observational study. *Mult Scler* 2013;19 1913-22.

4. Kasser SL, Jacobs JV, Foley JT et al. A prospective evaluation of balance, gait, and strength to predict falling in women with multiple sclerosis. *Arch Physical Med Rehabil* 2011;92:1840-6.

 Prosperini L, Kouleridou A, Petsas N et al. The relationship between infratentorial lesions, balance deficit and accidental falls in multiple sclerosis. *J Neurological Sci* 2011;304:55-60.

6. Matsuda PN, Shumway-Cook A, Bamer AM et al. Falls in multiple sclerosis. *PM&R* 2011;3:624-32.

7. Cattaneo D, De Nuzzo C, Fascia T et al. Risks of falls in subjects with multiple sclerosis. *Arch Physical Med Rehabil* 2002;83:864-7.

8. Gunn HJ, Newell P, Haas B et al. Identification of risk factors for falls in multiple sclerosis: a systematic review and meta-analysis. *Phys Ther* 2013;93:504-13.

9. Finlayson ML, Peterson EW, Cho CC. Risk factors for falling among people aged 45 to 90 years with multiple sclerosis. *Arch Physical Med Rehabil* 2006;87:1274-9.

10. Peterson EW, Cho CC, von Koch L et al. Injurious falls among middle aged and older adults with multiple sclerosis. *Arch Physical Med Rehabil* 2008;89:1031-7.

11. Coote S, Hogan N, Franklin S. Falls in people with multiple sclerosis who use a walking aid: prevalence, factors, and effect of strength and balance interventions. *Arch Physical Med Rehabil* 2013;94:616-21.

12. Cattaneo D, Regola A, Meotti M. Validity of six balance disorders scales in persons with multiple sclerosis. *Disability Rehabil* 2006;28:789-95.

13. Sosnoff JJ, Socie MJ, Boes MK et al. Mobility, balance and falls in persons with multiple sclerosis. *PloS one* 2011; 6: e28021.

14. Nilsagard Y, Lundholm C, Denison E et al. Predicting accidental falls in people with multiple sclerosis -- a longitudinal study. *Clin Rehabil* 2009;23:259-69.

15. Prosperini L, Fortuna D, Gianni C et al. The diagnostic accuracy of static posturography in predicting accidental falls in people with multiple sclerosis. *Neurorehabil Neural Repair* 2013;27:45-52.

16. Pardasaney PK, Latham NK, Jette AM et al. Sensitivity to change and responsiveness of four balance measures for community-dwelling older adults. *Phys Ther* 2012;92:388-97.

17. Schoene D, Wu SM, Mikolaizak AS et al. Discriminative ability and predictive validity of the timed up and go test in identifying older people who fall: systematic review and meta-analysis. *J Am Geriatr Soc* 2013;61:202-8.

18. Lord SR, Menz HB, Tiedemann A. A physiological profile approach to falls risk assessment and prevention. *Phy Ther* 2003;83:237-52.

 Hohol MJ, Orav EJ, Weiner HL. Disease steps in multiple sclerosis: a longitudinal study comparing disease steps and EDSS to evaluate disease progression. *Mult Scler* 1999;5:349-54.

20. Lechner-Scott J, Kappos L, Hofman M et al. Can the Expanded Disability Status Scale be assessed by telephone? *Mult Scler* 2003;9:154-9.

21. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology* 1983;33:1444-52.

22. Zajicek JP, Ingram WM, Vickery J et al. Patient-orientated longitudinal study of multiple sclerosis in south west England (The South West Impact of Multiple Sclerosis Project, SWIMS) 1: protocol and baseline characteristics of cohort. *BMC Neurol* 2010;10:88.

23. Anstey KJ, Wood J, Kerr G et al. Different cognitive profiles for single compared with recurrent fallers without dementia. *Neuropsychol* 2009;23:500-8.

24. Lord SR, Ward JA. Age-associated differences in sensori-motor function and balance in community dwelling women. *Age Ageing* 1994;23:452-60.

25. Low Choy NL, Brauer SG, Nitz JC. Age-related changes in strength and somatosensation during midlife: rationale for targeted preventive intervention programs. *Ann New York Acad Sci* 2007;1114:180-93.

26. Choy NL, Brauer S, Nitz J. Linking stability to demographics, strength and sensory system function in women over 40 to support pre-emptive preventive intervention. *Climacteric* 2008;11:144-54.

27. Illing S, Choy NL, Nitz J et al. Sensory system function and postural stability in men aged 30-80 years. *Aging Male* 2010;13:202-10.

28. Nolan M, Nitz J, Choy NL, Illing S. Age-related changes in musculoskeletal function, balance and mobility measures in men aged 30-80 years. *Aging Male* 2010;13:194-201.

29. Molloy DW, Alemayehu E, Roberts R. Reliability of a Standardized Mini-Mental State Examination compared with the traditional Mini-Mental State Examination. *Am J Psychiat* 1991;148:102-5.

30. Gibson MJ, Isaacs B, Radebaugh T et al. The prevention of falls in later life. A report of the Kellogg International Work Group on the prevention of falls by the elderly. *Dan Med Bull* 1987;34:1-24.

31. Lamb SE, Jorstad-Stein EC, Hauer K et al. Development of a common outcome data set for fall injury prevention trials: the Prevention of Falls Network Europe consensus. *J Am Geriatr Soc* 2005;53:1618-22.

32. Perry L, Kendrick D, Morris R et al. Completion and return of fall diaries varies with participants' level of education, first language, and baseline fall risk. J Gerontol: *Biol Med Sci* 2012;67:210-4.